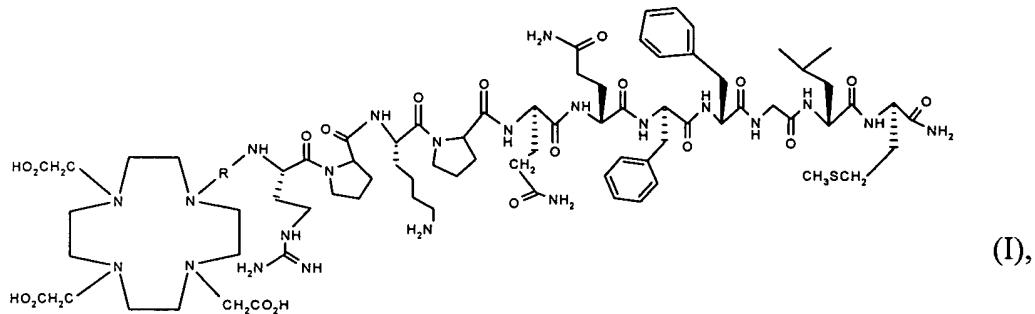


AMENDMENTS TO THE CLAIMS

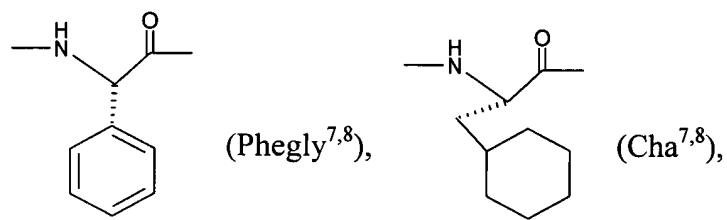
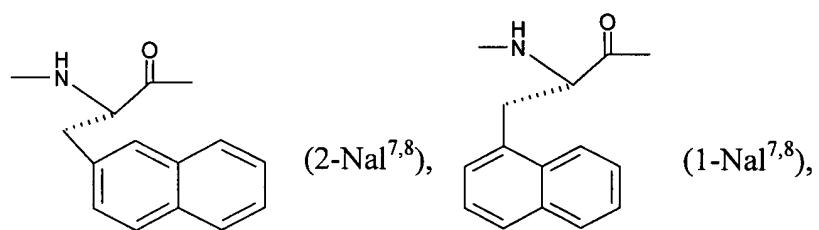
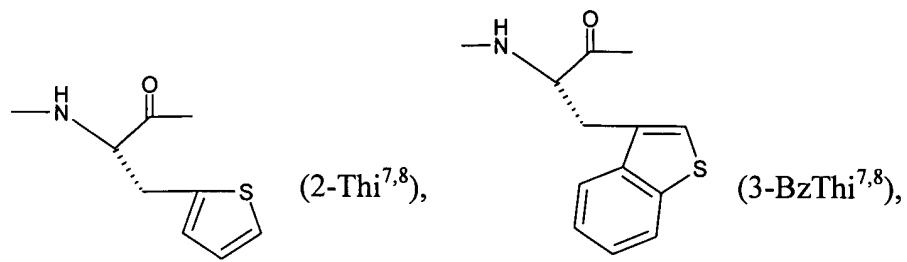
Claim 1. (Currently Amended) Use of A method of targeting a brain tumor, localizing or treating a brain tumor or a satellite lesion thereof in a host afflicted with brain tumor, comprising administering to the host a radio-nuclide labelled conjugates conjugate of substance P and a chelator molecule, having the abbreviation Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and comprising compounds the structure of formula I



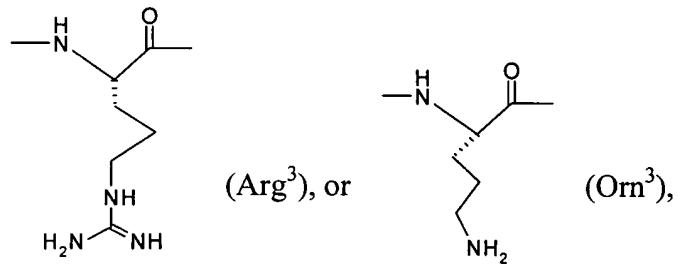
wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-, or an analogue of formula I with at least one of the subsequent following modifications in the amino acid sequence of substance P:

- a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by - N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar), and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149, as active ingredient in radiopharmaceutical or radio-diagnostic formulations for targeting or treating brain tumors, especially gliomas.

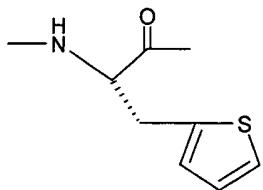
Claim 2. (Currently Amended) Use The method according to claim 1, wherein the amino acid sequence ~~in formula I corresponds to formulae of substance P is:~~

- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH₂,
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O₂)-NH₂,
- c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH₂,
- d) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH₂,
- e) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH₂,
- f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂,
- g) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂,
- h) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met(O₂)-NH₂,
- i) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O₂)-NH₂,
- j) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met-NH₂,
- k) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met(O₂)-NH₂
- l) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met-NH₂,
- m) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met(O₂)-NH₂,
- n) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH₂, or
- o) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met(O₂)-NH₂.

Claim 3. (Currently Amended) Use The method according to claim 1, wherein the compounds compound of formula I comprise comprises in the 11-position of the amino acid sequence of the natural substance P sequence a methioninsulfone methionine sulfone residue of formula -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- instead of a methionin methionine residue.

Claim 4. (Currently Amended) Use The method according to claim 1, wherein the glycine glycine residue in position 9 of the amino acid sequence of the natural substance P sequence is replaced by a sarcosin sarcosine residue of formula -N(CH₃)-CH₂-C(O)-.

Claim 5. (Currently Amended) Use The method according to claim 1, wherein the phenylalanine residue in the 7- or 8-position or in both said positions of the amino acid sequence of natural substance P sequence is replaced by a 3-(2-thienyl)-alanine residue of formula



Claim 6. (Currently Amended) Use The method according to claim 1, wherein the phenylalanine residue in the 8-position of the amino acid sequence of natural substance P sequence is replaced by a 3-(2-thienyl)-alanine and the glycine glycine residue in position 9 is replaced by a sarcosine residue.

Claim 7. (Currently Amended) Use The method according to claim 1, wherein the ~~methionin~~ methionine residue in the 11-position of the amino acid sequence of natural substance P sequence is replaced by a ~~methioninsulfone~~ methionine sulfone residue, and the phenylalanine residue in the 8-position of the natural substance P sequence is replaced by a 3-(2-thienyl)-alanine residue, or the ~~glyein~~ glycine residue in position 9 is replaced by a sarcosine residue.

Claim 8. (Currently Amended) Use The method according to claim 1, wherein the amino acid sequence in formula I ~~corresponds to formulae is:~~

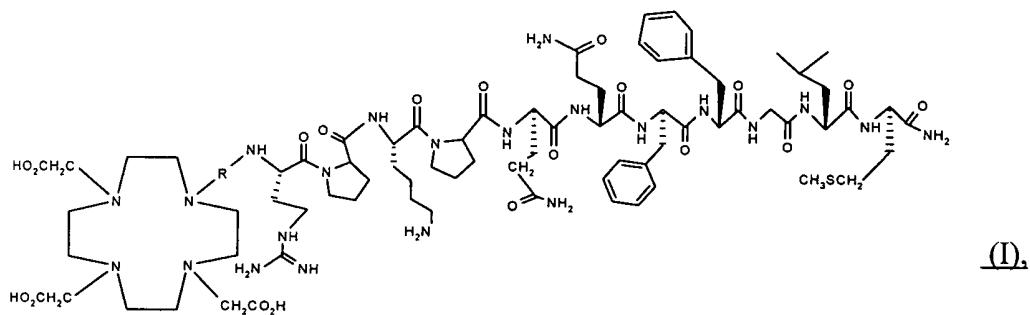
- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O₂)-NH₂,
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH₂,
- c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH₂,
- d) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH₂,
- e) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂,
- f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂,
- g) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH₂, or
- h) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O₂)-NH₂.

Claim 9. (Currently Amended) Use The method according to claim 1, wherein the amino acid sequence in formula I ~~corresponds to formulae is:~~

- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂, or
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂.

Claim 10. (Currently Amended) A method of targeting a brain tumors tumor, localizing or treating a brain tumors and the tumor or a satellite lesions lesion thereof in a host afflicted with brain tumors, e.g. gliomas, in administering tumor, which comprises administering to the host at least one compound conjugate of substance P and a chelator molecule, having the abbreviation

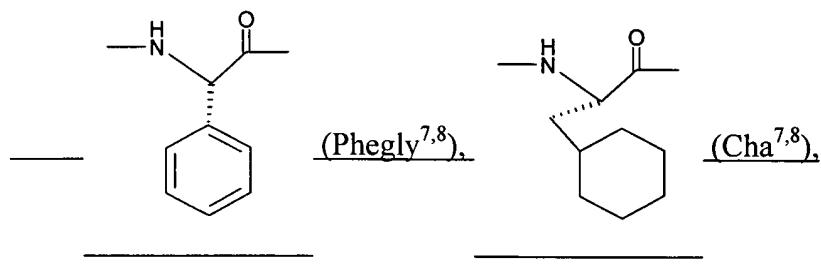
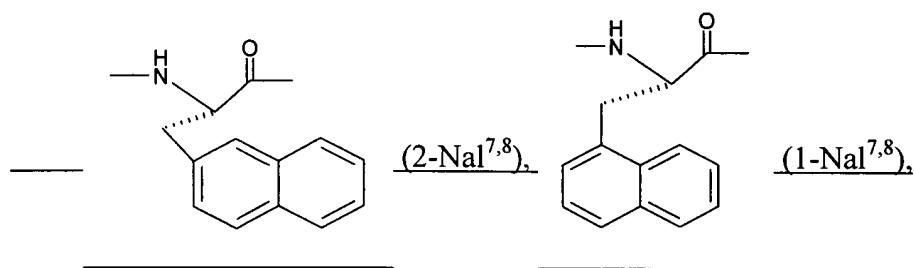
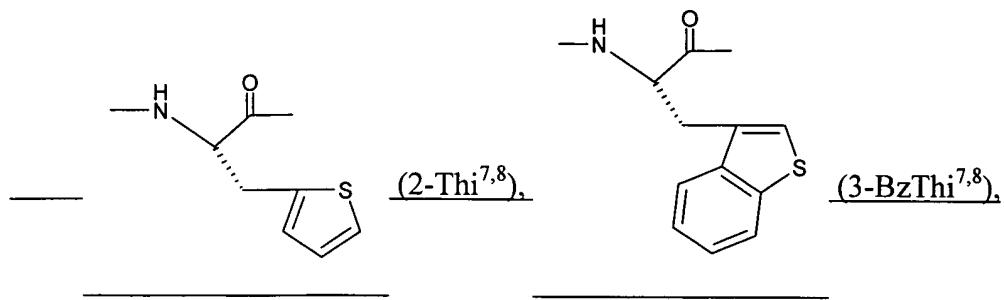
Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



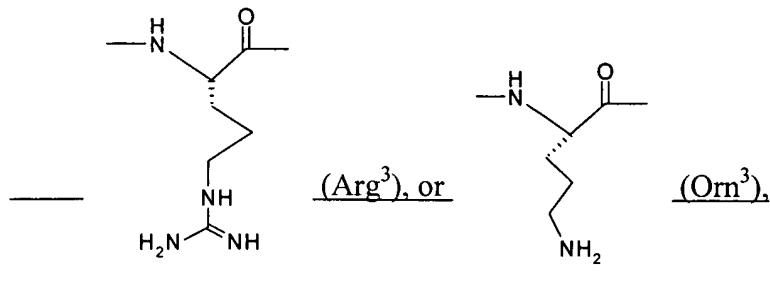
wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

- a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



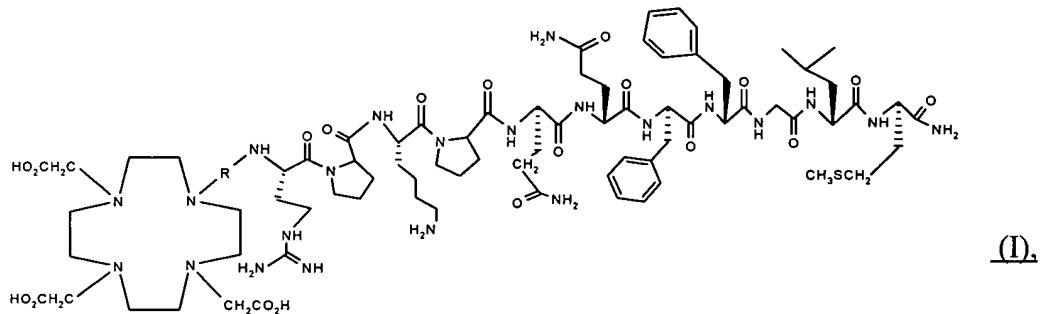
e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar).
or an analogue of a compound of formula I.

Claim 11. (Currently Amended) A therapeutic or diagnostic method for targeting a brain tumors tumor, localizing or treating a brain tumors and the tumor or a satellite lesions lesion thereof in a mammal mammal, comprising administering to a mammal in need of such therapy, an effective amount of a radio-nuclide labelled conjugate of substance P conjugate of and a chelator molecule, having the abbreviation Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I

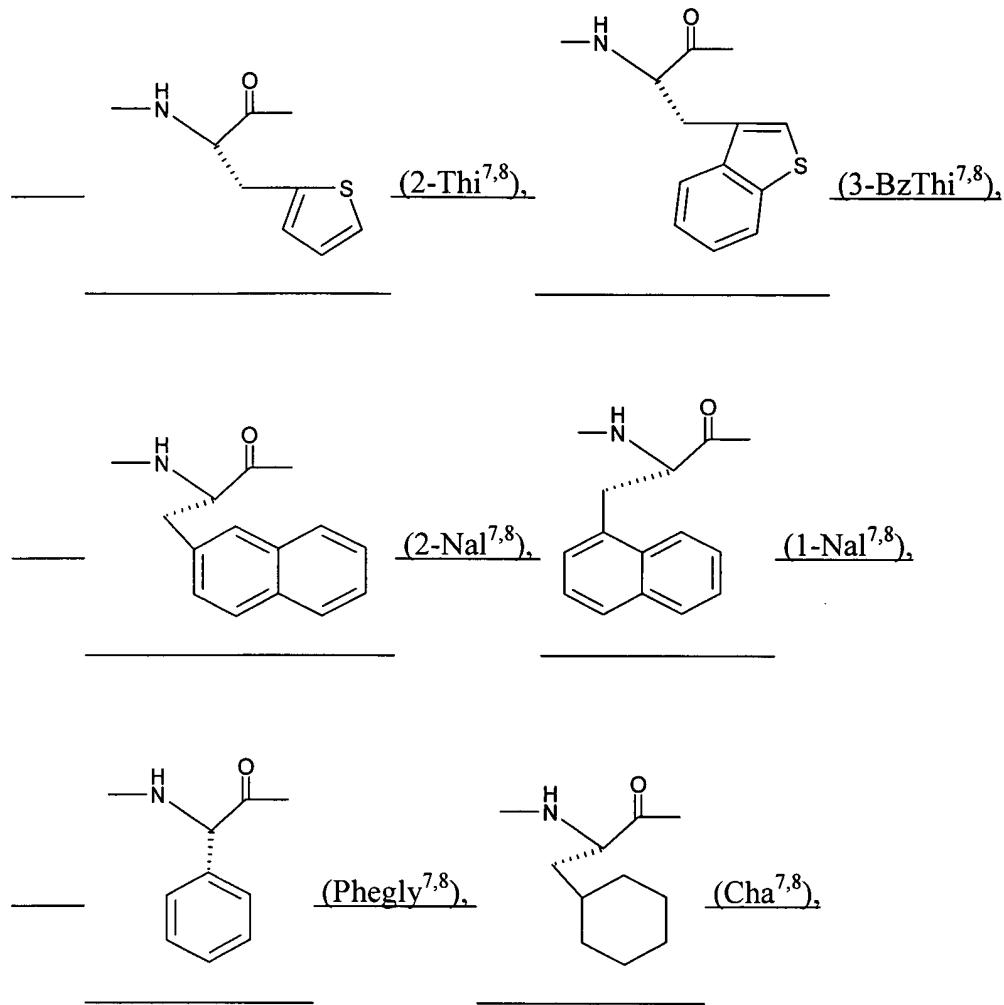


wherein

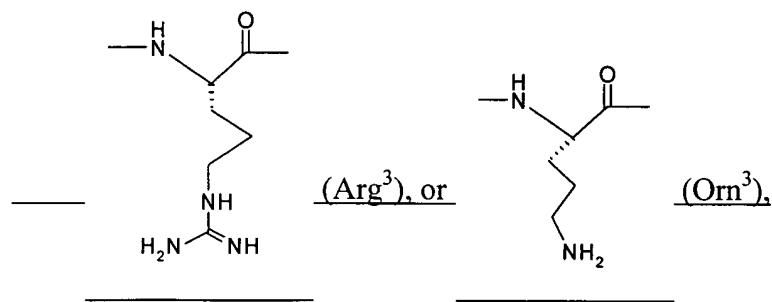
R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-, or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

- replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae

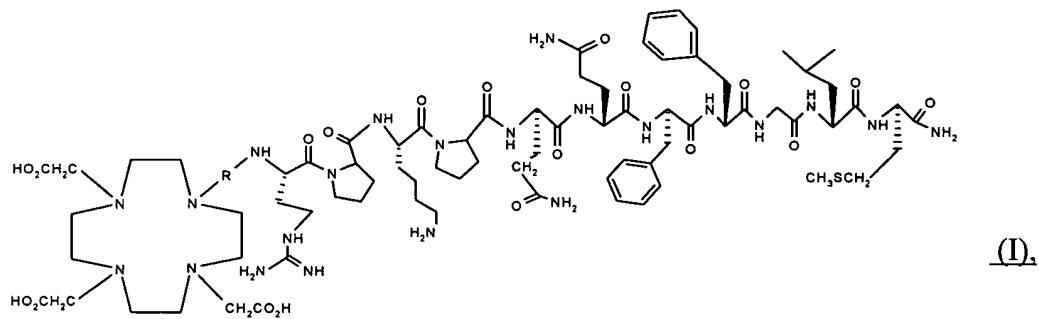


e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or
 g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -
N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),
 and wherein the conjugate is labelled with a radio-nuclide selected from the group
 consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67,
Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-
86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166,
Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.
 or an analogue thereof.

Claim 12. (Currently Amended) A method of delivering a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof to a host, comprising administering to a host a radio-nuclide labelled conjugate of substance P conjugate of and a chelator molecule, having the abbreviation
Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

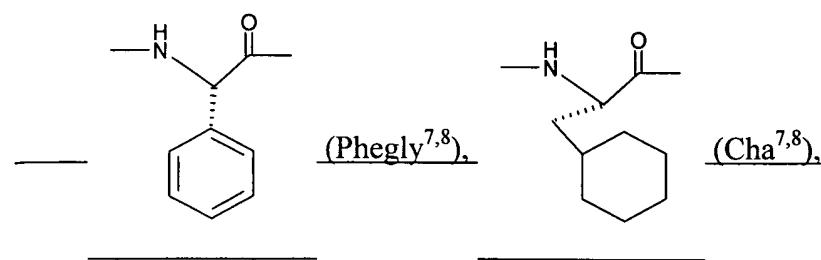
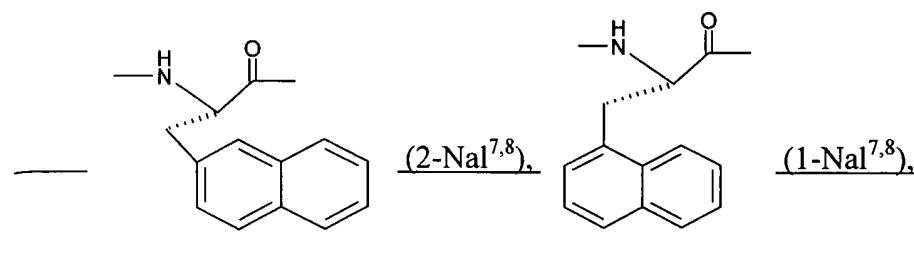
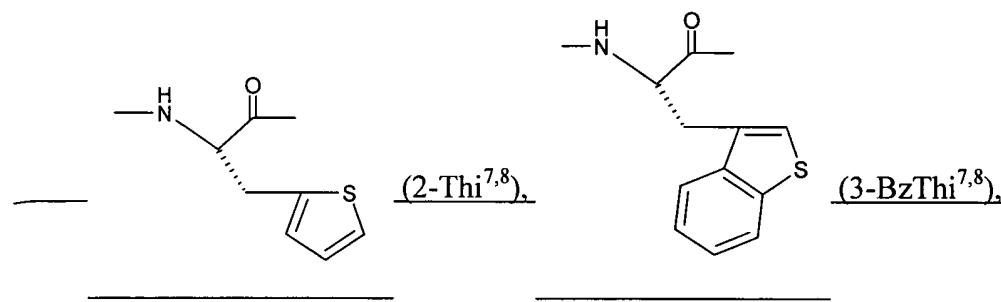
a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),

-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),

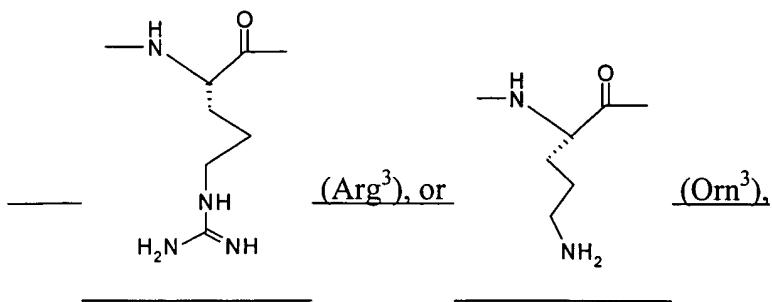
b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),

c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



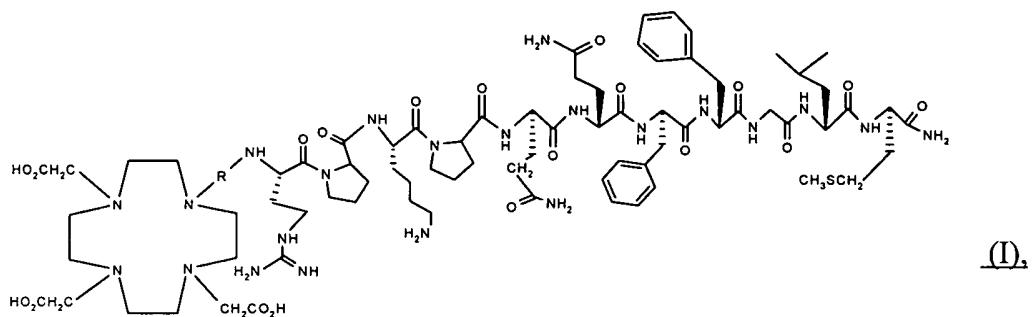
e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or
g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -
N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),
and wherein the conjugate is labeled with a radio-nuclide selected from the group
consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67,
Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-
86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166,
Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149,
or an analogue thereof.

Claim 13. (Currently Amended) A method Use of a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof for the manufacture of a medicament useful for the detection and therapeutic treatment of a brain tumors and tumor or satellite lesions lesion thereof in an a mammal, such as a human, which comprises mixing a radio-nuclide labelled conjugate of substance P and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,

or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

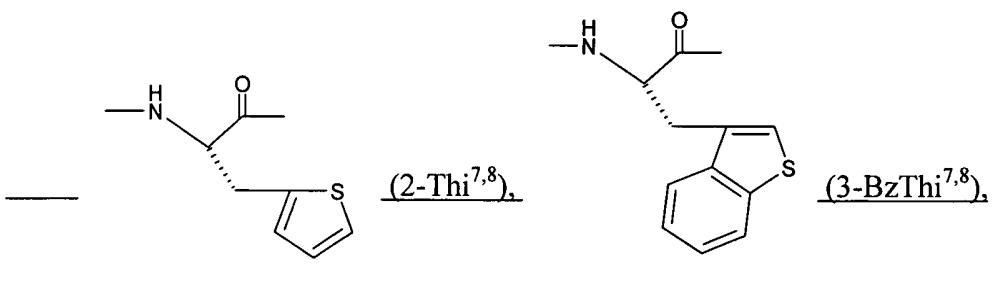
a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),

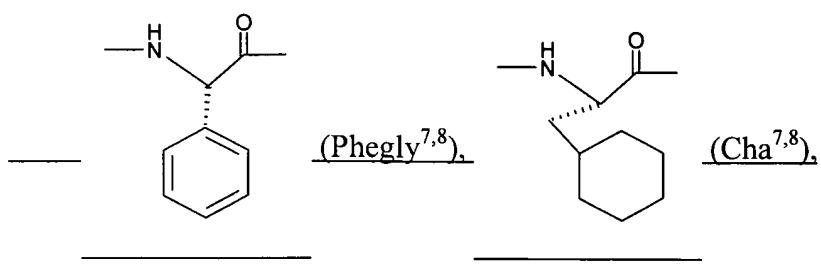
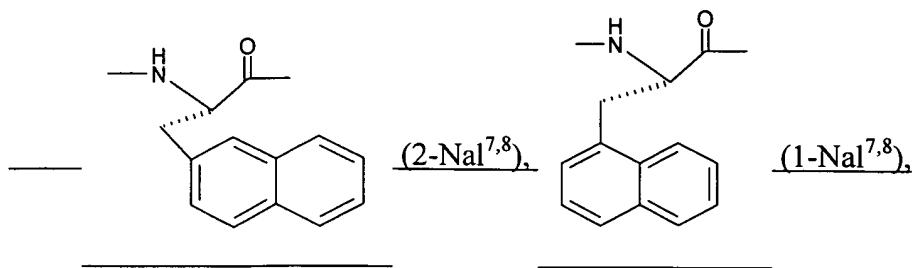
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),

b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),

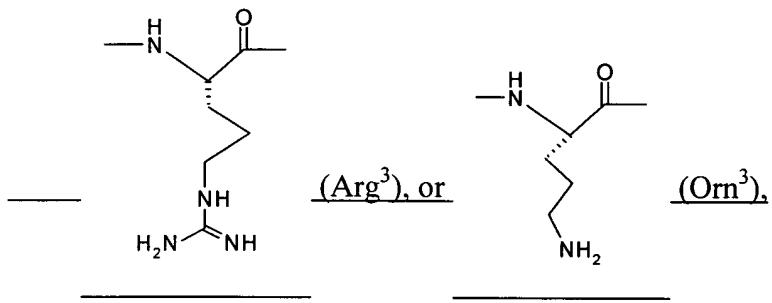
c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae





e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -

N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),

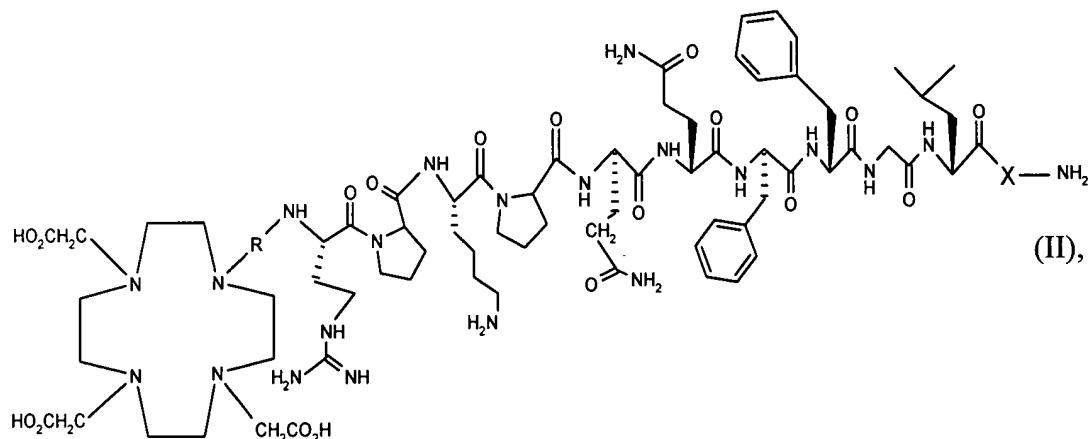
and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149;

with a pharmaceutical carrier.

Claims 14-16. (Cancelled)

Claim 17. (New) A conjugate of a substance P analogue and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-X¹¹-NH₂ and the structure of formula II



wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)- and

X is -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹), -NH-

CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-

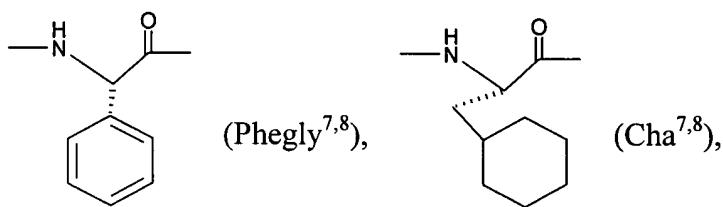
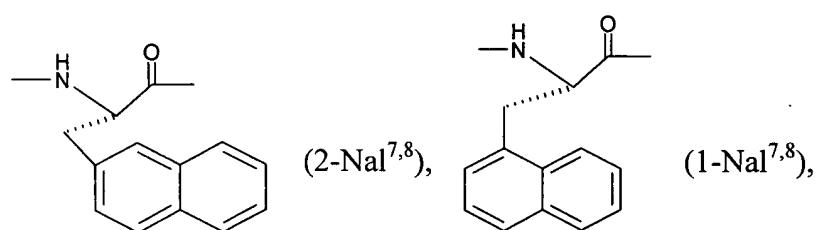
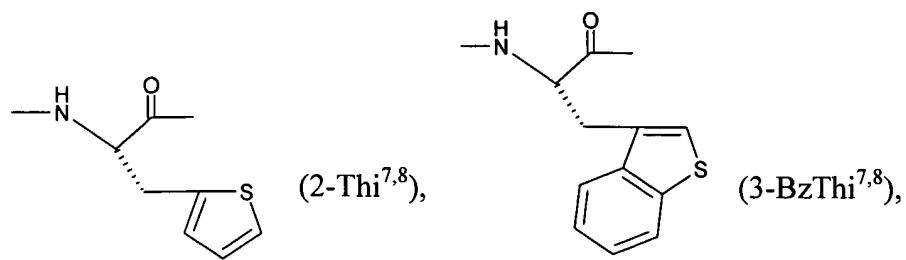
CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),

or an analogue of formula II with at least one of the following modifications in the amino acid sequence of substance P analogue:

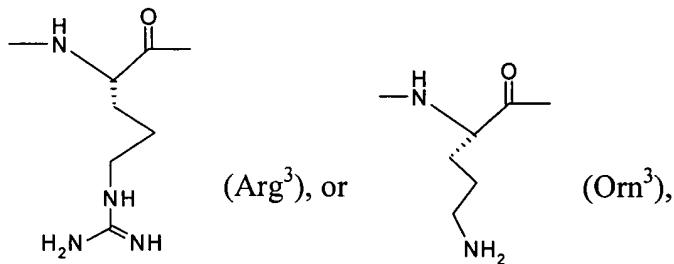
a) replacement of Leu¹⁰ by -NH-CH(CH(CH₃)CH₂CH₃)-C(O)- (hereinafter abbreviated Ile¹⁰),

b) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

c) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



d) replacement of Lys³ by residue of formulae



e) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or
 f) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by
 -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),

and wherein the conjugate is unlabelled or labeled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

Claim 18. (New) The conjugate of claim 17 wherein

X is -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹).

Claim 19. (New) A composition comprising at least one pharmaceutical carrier and at least one conjugate according to claim 17.

Claim 20. (New) A composition comprising at least one pharmaceutical carrier and at least one conjugate according to claim 18.

Claim 21. (New) A method of targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, comprising administering to the host a conjugate of claim 17.

Claim 22. (New) A method of targeting a glioma or treating a glioma in a host afflicted with glioma, comprising administering to the host a conjugate of claim 17.

Claim 23. (New) A method of targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, comprising administering to the host a conjugate of claim 18.

Claim 24. (New) A method of targeting a glioma or treating a glioma in a host afflicted with glioma, comprising administering to the host a conjugate of claim 18.

Claim 25. (New) The method of claim 21, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 26. (New) The method of claim 22, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 27. (New) The method of claim 23, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 28. (New) The method of claim 24, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 29. (New) A method for the manufacture of a radiopharmaceutical or radio-diagnostic formulation useful for targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, which comprises a radio-nuclide labeled conjugate of claim 17.

Claim 30. (New) A method for the manufacture of a radiopharmaceutical or radio-diagnostic formulation useful for targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, which comprises a radio-nuclide labeled conjugate of claim 18.